

**BREACH**  
BELGIAN RESEARCH AIDS&HIV CONSORTIUM



## Best Poster Contest

### **11 Posters**

- 3 Basic Science
- 6 Clinical Science
- 2 Public Health



# Towards a functional cure for HIV-1 infection: BRD4 modulator ZL0580 and LEDGINs additively block and lock HIV-1 transcription

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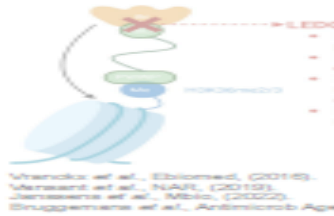


## INTRODUCTION

Residual transcriptional activity after LEDGIN-treatment

BRD4 regulates enhancer activity

Effect of BRD4 modulators on HIV-1 transcription



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## METHODS AND RESULTS

### Basic Science

1. JQ1 promotes and ZL0580 hampers HIV-1 transcription and reactivation in SupT1 cells

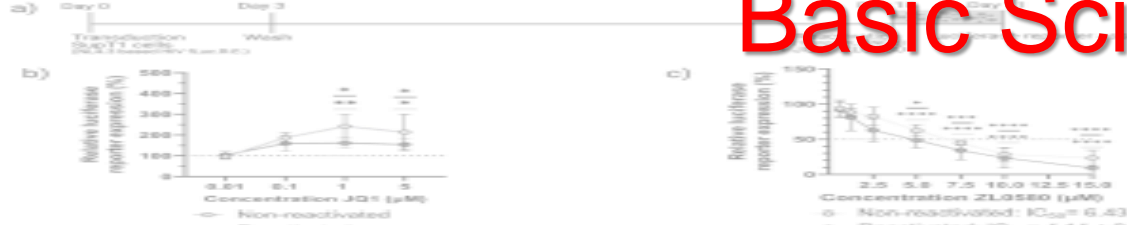


Figure 1. HIV-1 transcription and reactivation in SupT1 cells. (a) HIV-1 transcription and reactivation in SupT1 cells. (b) JQ1 promotes HIV-1 transcription and reactivation in SupT1 cells. (c) ZL0580 hampers HIV-1 transcription and reactivation in SupT1 cells.

2. JQ1 ↑ and ZL0580 ↓ the co-localization of BRD4 with acetylated histones

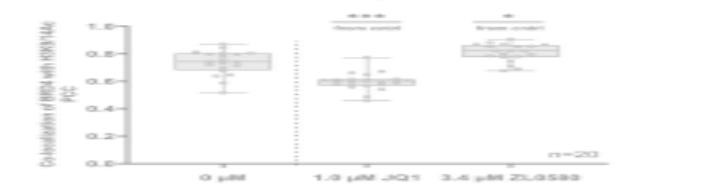


Figure 2. SupT1 cells were left untreated or incubated with JQ1/ZL0580 for 24h. After confocal imaging, quantification of the BRD4-H3K9Ac/ACT4 co-localization was performed using Pearson correlation coefficient (PCC). The correlation coefficient (PCC) represents the correlation between the two channels. PCC values range from -1 (no correlation) to 1 (perfect correlation). PCC values were compared to the untreated control using a two-tailed t-test.

## “TOWARDS A FUNCTIONAL CURE FOR HIV-1 INFECTION : BRD4 MODULATOR ZL0580 AND LEDGINs ADDITIVELY BLOCK AND LOCK HIV-1 TRANSCRIPTION ”

3. Drug-drug interaction



Figure 3. Infection experiments were conducted as described in Figure 1A, but a dilution series of LEDGIN CX014442 was added during transcription. (a) Heatmap of drug-drug interaction between JQ1 and CX014442. (b) Heatmap of drug-drug interaction between ZL0580 and CX014442.

4. LEDGINs and ZL0580 synergistically block HIV-1 transcription in primary cells infected *in vitro*



Figure 4. (a) Timeline of experiment. (b) Relative luciferase reporter expression (%) was calculated by dividing the untreated control (0 μM ZL0580). For statistical analysis, a One-way ANOVA test was performed (\*, P < 0.05; \*\*, P < 0.01; \*\*\*, P < 0.001). The luciferase reporter assay showed that ZL0580 synergistically blocks HIV-1 transcription in primary cells. ZL0580 synergistically blocks HIV-1 transcription in primary cells.

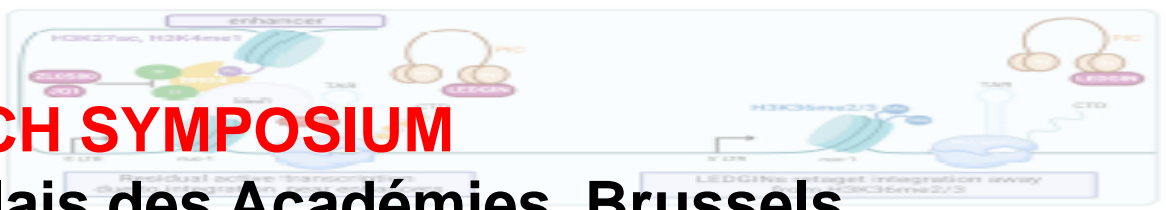
Eline Pellaers, Alexe Denis, Wout Hannes, Anayat Bhat, Julie Janssens, Zhang Peng, Zeger Debyser

## CONCLUSION

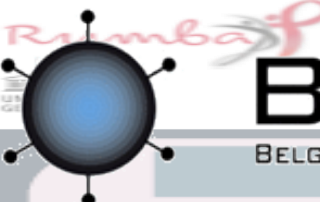
- BRD4 can be modulated to both activate (JQ1) and inhibit (ZL0580) HIV-1 transcription and reactivation
- JQ1 and ZL0580 oppositely affect the binding of BRD4 to acetylated chromatin
- ZL0580 blocks HIV-1 transcription in primary cells
- Enhancers may drive residual expression after LEDGIN-treatment
- ZL0580 and LEDGINs are a promising 'latency-purging cocktail' to enhance the efficiency of the block-and-lock functional cure strategy

## 12<sup>th</sup> BREACH SYMPOSIUM

November 28<sup>th</sup>, 2024, Palais des Académies, Brussels



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### BACKGROUND

- TANCO
- SALSA
- DYAD

Above switch-studies showed no inferior virologic efficacy DTG/3TC versus 3/4 drug regimens. 2<sup>nd</sup> generation integrase inhibitors (INSTI) have been associated with weight gain.

Weight gain ? Lipid changes ? Impact of NRTI

### MATERIALS & METHODS

- RUMBA study: Phase 4 RCT with analysis of viral reservoir as primary endpoint
- Virologic suppressed participants were 2:1 randomized to switch to DTG/3TC or stay on B/F/TAF
- W48 virologic, metabolic, and body composition outcomes
- Differences in metabolic outcomes between W144 and baseline are reported here

## Clinical Science

### “RUMBA’S WEEK 144 RESULTS CONFIRM REASSURING METABOLIC OUTCOMES IN BOTH DTG/3TC AND B/FTC/TAF”

#### Population

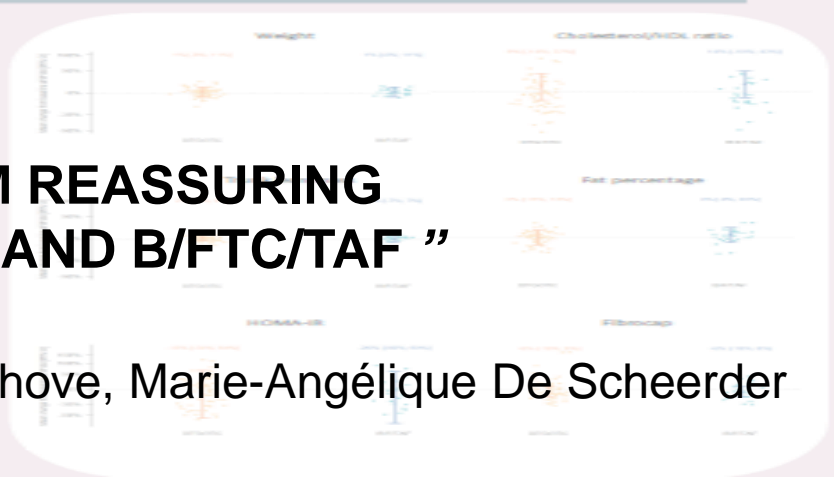
	Total (n=134)	B/F/TAF (n=43)	DTG/3TC (n=47)
Sex, M/F	118/12	38/5	70/8
Ethnicity, European/Asian/Other	102/14/14	32/5/6	70/8/8
Age, y, median (IQR)	47 (37-55)	45 (37-55)	49 (40-55)
Time on ART, y, median (IQR)	7.2 (4.5-10.4)	7.2 (4.5-10.4)	7.2 (4.5-10.4)
BMI, kg/m <sup>2</sup> , median (IQR)	25 (23-28)	25 (23-28)	25 (23-28)
INSTI, median (IQR) <1y on 2 <sup>nd</sup> gen (INSTI)	15 (4-11)	5 (1-11)	11 (4-11)
TAF, naive / <1y on TAF	49/11	15/3	34/8

Baseline characteristics of the RUMBA participants

#### Outcomes

	Treatment ratio (95% CI)			B/F/TAF			DTG/3TC		
	Estimate	95% LCI	95% UCI	Estimate	95% LCI	95% UCI	Estimate	95% LCI	95% UCI
Weight	1.04	0.98	1.04	1.04	0.93	1.11	1.05	0.92	1.11
Cholesterol (LDL)	1.04	0.93	1.15	1.14	0.9	1.42	1.09	0.85	1.37
Trunk lean mass	1.04	0.93	1.15	1.04	0.93	1.15	1.04	0.93	1.15
Fat percentage	1.04	0.93	1.15	1.04	0.93	1.15	1.04	0.93	1.15
HOMA-IR	0.93	0.85	1.05	0.9	0.4	1.6	0.87	0.48	1.54
FibroCap	1	0.93	1.06	0.94	0.81	1.06	0.94	0.82	1.06

Metabolic changes after 144 weeks, corrected for baseline response value, baseline regimen and baseline BMI. LCI, Lower confidence interval; UCI, Upper confidence interval [ref].



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### RUMBA versus other DTG/3TC trials

- TANCO** (n=74)
  - W48: 50% switch of TAF in DTG/3TC group
  - Prior regimen: 70% INSTI; 100% TAF
  - RUMBA: 50% switch of TAF in DTG/3TC group
  - No differences in lipid found
- SALSA** (n=83)
  - W48: More weight gain in DTG/3TC vs 3-4DR (adjusted weight difference: 1.2kg)
  - 40% INSTI; 50% 2<sup>nd</sup> gen INSTI; 30% TAF; 40% TDF
  - RUMBA: no TDF-containing baseline regimens
- PASO DOBLE** (n=63)
  - W48: No differences in weight between DTG/3TC and 3-4DR
  - Way to improve starting DTG/3TC in TDF
  - RUMBA: W48: No differences in weight between DTG/3TC and 3-4DR
  - Way to improve starting DTG/3TC in TDF
- DYAD** (n=60)
  - W48: No differences in weight between DTG/3TC and 3-4DR
  - RUMBA: W48: No differences in weight between DTG/3TC and 3-4DR
  - Way to improve starting DTG/3TC in TDF

### CONCLUSIONS & CONSIDERATIONS

- RUMBA's week 48 data showed that switching to DTG/3TC had no impact on the viral reservoir. Metabolic outcomes were comparable between 2DR and 3DR, with slightly better body composition measures in 2DR [1].
- At week 144, we confirm reassuring metabolic outcomes in both the DTG/3TC and B/F/TAF group. No statistically significant differences are found.
- Metabolic outcomes in DTG/3TC switch trials depend mostly on baseline regimen.
- Metabolic outcomes should be further investigated to better understand their role and impact in people with increased risk of metabolic comorbidity.
- RUMBA W144 analyses, with multiple imputations based on all intermediate data (week 72, 96 and 120) as well as W240 data.

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Despite the availability of a range of effective HIV prevention tools, new HIV acquisition continue to occur mainly in minority populations. Therefore, we need to better understand the role of the environmental and social context in how these new HIV acquisitions happen. Qualitative social network analysis is an approach to explore how people's social and sexual may influence HIV acquisition and prevention behaviors.

Friends, family members, regular sex partners and HIV physicians were placed closest to the ego (=the participant) on the sociogram.  
• Self-identified gay men did not consider their casual sex partners as emotionally close enough to be included in the sociogram, even though these partners were often participants' primary source of information about safer sex.  
• HIV disclosure to a partner was often related to increased sexual risk-taking under influence of drugs.  
• Men who had sex with men (MSM) were more likely to disclose their HIV status to their partners than heterosexual men.  
• Most participants only disclosed HIV to those closest to them, and the amount of disclosure was influenced by lack of social support.  
• Feelings of internalized HIV stigma and homophobia prevented HIV disclosure, especially among heterosexuals and heterosexual and bisexual MSM.

"Social pressure might be a bit of a heavy term, but it was almost normal that when we went out, drugs would be used. (...) I felt that it made me less likely to say 'no' when I would have said 'no' if I hadn't been under the influence. Under influence, I didn't say it as quickly. Not because others encouraged me, but because of the influence of those drugs." (gMSM)

"The diagnosis in itself made it clear to me who I wanted to inform. The people I felt I needed to know because it's the people I am close to and spend time with" (gMSM)

"Besides the few people who only talk about my HIV because I am also afraid to be confronted with it, I am not a person like in the clichés of unsafe behavior and decadence etc. I like to go out and dance. I also took drugs, xtc, coke and alcohol from time to time, but never to the extent that I led a normless life, quite the contrary. No, the problem is that if I tell my friends or family that I am HIV positive than I will be stigmatized as gay. I am not gay because I do not like men, I only have sex with men" (hMSM)

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## Public Health

### OBJECTIVE

- To describe social and sexual networks (SSN) among people newly diagnosed with HIV
- To understand the influence of SSN on preventive and risk behavior
- To describe perceptions on how participants acquired HIV

### METHODOLOGY

- Design**
- Qualitative sub-study of COLIBRI (Connecting Laboratory Information with Behaviour for Recent and Advanced Infection) (Vanden Bulcke et al., 2024)
  - Ego-centric social network approach
  - In-depth interviews
  - Constructing of sociograms of social and sexual networks
- Participants**
- N=20 participants who were newly diagnosed with HIV and currently in follow-up at Ghent University Hospital
  - n=13 identified as gay MSM (gMSM); n=2 as heterosexual men who have sex with women (hMSW); n=1 as a heterosexual men who only has sex with men (hMSM); n=1 as heterosexual woman who has sex with men (hWSM); n=3 as bisexual men who only have sex with men (bMSM)
- Analysis**
- Descriptive analysis of sociogram structure
  - Reflexive thematic analysis of interview data

## "SOCIAL AND SEXUAL NETWORKS OF NEWLY DIAGNOSED PEOPLE LIVING WITH HIV - A QUALITATIVE SOCIAL NETWORK ANALYSIS"

Ella Van Landeghem, Charlotte Vanden Bulcke, Anke Rotsaert, Jessika Deblonde, Chris Verhofstede, Christiana Nöstlinger

### SOCIOGRAMS

Examples of pseudonimized and digitalized visualisations of sociograms constructed during the in-depth interviews



### CONCLUSION

- Important differences in the social and sexual networks of gay, bisexual and bisexual identified MSM influencing sexual risk taking and prevention behavior
- Future prevention initiatives should be tailored to the needs of people who do not identify as the established transmission groups
- Awareness of biomedical prevention should be raised in the general population, providing a base on which more tailored promotion can be built.
- Involving family physicians and social empowering people living with HIV may help to decrease (anticipated) HIV stigma.

References: Vanden Bulcke, C., Deblonde, J., Necoș, C., Van Praet, J., Van Cutsem, E., Mertens, L., ... & Verhofstede, C. (2024). Profile of Persons Recently Infected with HIV-1 in Belgium: New Insights to Tailor Prevention Efforts. *AIDS and Behavior*, 1-12.



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